REMARKS

I. Status of the Specification and Claims

As requested by the Examiner, the Specification has been amended to properly reflect information regarding related applications and priority claims. No amendments to the claims have been made. Claims 1 and 4-5 are pending.

II. Rejection Under 35 USC 103

Claims 1 and 4-5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Roth (US 5,273,995) in view of Lee et al. (US 5,489,611), Hunninghake et al., Wanner et al., and Medline abstract 96306618. Applicants respectfully traverse this rejection.

As set forth in MPEP 2142:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. ***Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.*** The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added)

The cited references, whether alone or in combination, fail to meet these standards and to provide such teaching, suggestion, incentive or inference such that one of skill in the art would be motivated to modify their teachings and arrive at Applicants' claimed invention with any reasonable expectation of success.

Applicants' claimed invention is directed to a pharmaceutical composition based on combination of two (2) compounds: (i) a retinoid Lp(a) inhibitor or a pharmaceutically acceptable salt thereof and (ii) atorvastatin or a pharmaceutically acceptable salt thereof. While each of the references cited by the Examiner may describe each of the claimed elements

independently, none of the cited references teach or suggest the combination of the two compounds into a single pharmaceutical composition with a suitable carrier or diluent.

As set forth in MPEP 2143.01:

> A statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" **because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.** *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). (Further emphasis added).

Here, Roth describes [R-(R*,R*)]-2-(4-fluorophenyl)-ß,ð-dihydroxy-5-((1-methylethyl)-3-phenyl-4-[(phenylamino)-carbonyl]-1H-pyrrole-1-heptanoic acid or (2R-trans)-5(4-fluorophenyl)-2-(1-methylethyl-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide; and pharmaceutically salts thereof (see Abstract). As recognized by the Examiner, Roth is silent as to a retinoid Lp(a) inhibitor or a pharmaceutically acceptable salt thereof.

Lee describes retinoids that are effective to lower plasma levels of Lp(a) in mammals (see Abstract). Lee is silent as to atorvastatin or a pharmaceutically acceptable salt thereof.

Hunninghake, Wanner, and the Medline abstract describe the effects of, respectively, pravastatin, simvastatin and fluvastatin on lipoprotein (a). However, Hunninghake, Wanner, and the Medline abstract are silent as to (1) atorvastatin or a pharmaceutically acceptable salt thereof and (ii) a retinoid Lp(a) inhibitor. Thus, these references would not teach or suggest a combination of atorvastatin or a pharmaceutically acceptable salt thereof with a retinoid Lp(a) inhibitor. Applicants do not recognize the relevance of Hunninghake, Wanner and the Medline abstract to the claimed invention as they do not teach or suggest either of the claimed elements or Applicants' claimed combination of a retinoid Lp(a) inhibitor or a pharmaceutically acceptable salt thereof with atorvastatin or a pharmaceutically acceptable salt thereof in a single

pharmaceutical composition with a suitable diluent or carrier. As such, Hunninghake, Wanner and the Medline abstract would not provide one of the ordinary skill in the art with the requisite motivation to combine their teachings with those of Roth and Lee and arrive at Applicants' claimed invention with any reasonable expectation of success.

Thus, while the cited references may describe elements of the claimed invention individually, none of the cited references teach or suggest Applicants' claimed invention or provide the requisite motivation or teaching to combine their teachings and arrive at Applicants' claimed invention with any reasonable expectation of success. Thus, as per *Ex Parte Levengood* above, a *prima facie* case of obviousness has not been established.

At best, since none of the cited references teach or suggest the claimed combination, an improper "obvious to try" rationale is being applied. However, the cited references provide no teaching or suggestion that the claimed combination would be successful.

Applicants' claimed invention is not obvious in view of the cited references. Applicants respectfully request the rejection be withdrawn.

III. Conclusion

Applicants respectfully request reconsideration of the subject application in view of the above amendment and remarks. The subject application is now in condition for allowance and early notice to that effect is respectfully solicited.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 23-0455. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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